



ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2020-0391; FRL-8991-01-OCSP]

Benzobicyclon; Pesticide Tolerances

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation increases a tolerance for residues of benzobicyclon in or on rice grain and removes any restriction on regional use. Gowan Company requested this tolerance increase under the Federal Food, Drug, and Cosmetic Act (FFDCA).

DATES: This regulation is effective [INSERT DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Objections and requests for hearings must be received on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*], and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2020-0391, is available at <http://www.regulations.gov> or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566-1744, and the telephone number for the OPP Docket is (703) 305-5805.

Due to the public health emergency, the EPA Docket Center (EPA/DC) and Reading Room is closed to visitors with limited exceptions. The staff continues to

provide customer service via email, phone, and webform. For the latest status information on EPA/DC services, docket access, visit <http://www.epa.gov/dockets>.

FOR FURTHER INFORMATION CONTACT: Marietta Echeverria, Acting Director, Registration Division (7505P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (703) 305-7090; email address: RDFRNotices@epa.gov.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them.

Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How Can I Get Electronic Access to Other Related Information?

You may access a frequently updated electronic version of EPA's tolerance regulations at 40 CFR part 180 through the Government Publishing Office's e-CFR site at http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl.

C. How Can I File an Objection or Hearing Request?

Under FFDCA section 408(g), 21 U.S.C. 346a(g), any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in

accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2020-0391 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing and must be received by the Hearing Clerk on or before [INSERT DATE 60 DAYS AFTER DATE OF PUBLICATION IN THE *FEDERAL REGISTER*]. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA-HQ-OPP-2020-0391, by one of the following methods:

- *Federal eRulemaking Portal*: <http://www.regulations.gov>. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.

- *Mail*: OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

- *Hand Delivery*: To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at <http://www.epa.gov/dockets/where-send-comments-epa-dockets>.

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at <http://www.epa.gov/dockets>.

II. Summary of Petitioned-For Tolerance

In the *Federal Register* of April 22, 2021 (86 FR 21317) (FRL-10022-59) EPA issued a document pursuant to FFDCa section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide petition (PP 0F8831) by Gowan Company, P.O. Box 5569, Yuma, AZ 85364. The petition requested to amend the tolerance in 40 CFR 180.693 for residues of the herbicide benzobicyclon in or on rice to 0.15 parts per million (ppm). That document referenced a summary of the petition prepared by Gowan, the petitioner, which is available in the docket, <http://www.regulations.gov>. There were no comments received in response to the notice of filing.

III. Aggregate Risk Assessment and Determination of Safety

Section 408(b)(2)(A)(i) of FFDCa allows EPA to establish a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the tolerance is “safe.” Section 408(b)(2)(A)(ii) of FFDCa defines “safe” to mean that “there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information.” This includes exposure through drinking water and in residential settings but does not include occupational exposure. Section 408(b)(2)(C) of FFDCa requires EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance and to “ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue...”

Consistent with FFDCa section 408(b)(2)(D), and the factors specified therein, EPA has reviewed the available scientific data and other relevant information in support of this action. EPA has sufficient data to assess the hazards of and to make a determination on aggregate exposure for benzobicyclon, including exposure resulting from the tolerance established by this action. EPA's assessment of exposures and risks associated with benzobicyclon follows.

In an effort to streamline its publications in the *Federal Register*, EPA is not reprinting sections that repeat what has been previously published for tolerance rulemaking of the same pesticide chemical. Where scientific information concerning a particular chemical remains unchanged, the content of those sections would not vary between tolerance rulemaking, and EPA considers referral back to those sections as sufficient to provide an explanation of the information EPA considered in making its safety determination for the new rulemaking.

EPA has previously published a tolerance rulemaking for benzobicyclon, in which EPA concluded, based on the available information, that there is a reasonable certainty that no harm would result from aggregate exposure to benzobicyclon and established a tolerance for residues of that chemical. See the benzobicyclon tolerance rulemaking published in the *Federal Register* of April 25, 2017 (82 FR 18995) (FRL-9961-02). EPA is incorporating previously published sections from that rulemaking that remain unchanged, as described further in this rulemaking.

Toxicological profile. There have been updates to the toxicological profile from the previous assessment. The parent compound, benzobicyclon, is a pro-pesticide, which means it requires hydrolysis of the thiophenyl group to generate the anticipated pesticidal active moiety, metabolite B (also referred to as 1315P-070). The toxicological database is considered complete for risk assessment purposes for both the parent, benzobicyclon, and metabolite B. The enzyme 4-hydroxyphenylpyruvate dioxygenase (HPPD) is involved in the catabolism of tyrosine, an essential amino acid for mammals. While benzobicyclon may be referred to as an HPPD inhibitor, typical HPPD-inhibiting effects are not observed in its toxicological database. However, metabolite B does exhibit HPPD-inhibiting effects and is therefore considered an HPPD-inhibiting chemical. The initiating event in the mode-of-action (MOA)/adverse-outcome pathway (AOP) for HPPD-inhibiting chemicals, including metabolite B, involves binding of the chemical to

the HPPD enzyme causing complete or virtually complete enzyme inhibition, which leads to a build-up of systemic tyrosine levels (tyrosinemia) and a spectrum of tyrosine-mediated effects. In laboratory animals, these have been identified as ocular and skeletal developmental effects. Species differences exist in laboratory animals related to the ability of a species to clear excess tyrosine from its system, which can impact its sensitivity to HPPD-inhibiting chemicals and its relevance for human health risk assessment. In this risk assessment, endpoints were selected for both benzobicyclon and metabolite B. Taking into account species differences, endpoints for human health risk assessment of HPPD inhibitors, including metabolite B, were selected from studies available in mice and dogs. Studies from other HPPD inhibitors were used for bridging to metabolite B as needed. Since benzobicyclon does not exhibit HPPD-inhibiting properties, endpoints were selected from the most sensitive species and effects in its database (not restricted to mice and dogs).

Benzobicyclon: An acute dietary endpoint was not selected for benzobicyclon, as there were no effects attributable to a single dose identified in the database. The chronic dietary, incidental oral, and inhalation endpoints were based on increased incidence of hydropic degeneration (basophilic cells) in the pituitary observed in the two-generation reproduction toxicity study in rats. A dermal endpoint was not selected since no hazard was identified in the dermal toxicity study and there was no evidence of increased quantitative susceptibility in the database. Benzobicyclon is classified as “Not Likely to be Carcinogenic to Humans” based on the absence of treatment-related tumors in two adequate rodent carcinogenicity studies.

Metabolite B: There were no effects attributable to a single dose available in the metabolite B database or in studies from other HPPD inhibitors; therefore, an acute dietary endpoint was not selected for metabolite B. The chronic dietary endpoint is based on gallstones, eosinophilic cytoplasmic alteration, subepithelial mixed cell infiltrate, and

dilatation in/of the gallbladder; hepatocellular vacuolation, hepatocellular hypertrophy, and increased liver weight in males and females; and papillary mineralization of the kidney and changes in hematological parameters indicative of anemia in females observed in the chronic/carcinogenicity study in mice from another HPPD chemical available for bridging (tembotrione). Since the only anticipated exposure is through drinking water, no additional points of departure (PODs) were selected for metabolite B. There are no carcinogenicity studies available for metabolite B; however, carcinogenicity studies are available for bridging for all of the other currently registered HPPD inhibitors. Overall, potential carcinogenicity is not a concern for the HPPD inhibitors, and the chronic dietary endpoint and POD for metabolite B is considered protective of any potential carcinogenicity.

Additional information is available in the docket for this action in the document titled “Benzobicyclon: Section 3 Risk Assessment for Proposed New Formulation, Increase to the Established Tolerance, and National Use Expansion on Rice” (hereafter, the “Benzobicyclon Human Health Risk Assessment”).

Toxicological points of departure/Levels of concern. For a summary of the Toxicological Points of Departure/Levels of Concern for benzobicyclon and metabolite B used for human health risk assessment, please reference section 4.6.3 on pages 25-27 of the “Benzobicyclon Human Health Risk Assessment”.

Exposure assessment. EPA’s dietary exposure assessments have been updated to include the additional exposure from the tolerance increase on rice grain and national use expansion.

No effects attributable to a single dose were observed for benzobicyclon or metabolite B; therefore, acute dietary exposure assessments were not conducted.

Based on the toxicological effects of benzobicyclon and metabolite B, separate chronic dietary exposure and risk assessments were conducted. The assessments were

conducted using Dietary Exposure Evaluation Model software with the Food Commodity Intake Database (DEEM-FCID) Version 3.16, which uses food consumption data from the U.S. Department of Agriculture's (USDA's) National Health and Nutrition Examination Survey, What We Eat in America, (NHANES/ WWEIA). This dietary survey was conducted from 2003 to 2008.

The benzobicyclon chronic dietary exposure assessment assumed tolerance-level residues for rice, 100 percent crop treated (PCT), and a modeled estimated drinking water concentration (EDWC) of 0.199 parts per billion (ppb). The DEEM default processing factor of 1.25 was used for both rice flour and rice bran.

There is no anticipated exposure in food to metabolite B. As metabolite B is only a residue of concern in drinking water, the chronic dietary exposure assessment was conducted for drinking water only. The chronic analysis used a modeled EDWC of 4.27 ppb and assumed 100 PCT.

There are no residential (non-occupational) exposures associated with benzobicyclon or metabolite B.

Cumulative exposure. The Agency is required to consider the cumulative risks of chemicals sharing a common mechanism of toxicity. The Agency has determined that the (p-hydroxyphenyl-pyruvate dioxygenase) HPPD inhibitors share a common mechanism of toxicity as discussed in the document titled "HPPD Inhibiting Herbicides: State of the Science," which is available in the docket for this action. As explained in that document, the members of this group of chemicals share the ability to bind to and inhibit the HPPD enzyme resulting in elevated systemic tyrosine levels and common apical outcomes that are mediated by tyrosine, including ocular and developmental effects. In 2021, after establishing a common mechanism grouping for the HPPD inhibitors, the Agency conducted the "P-Hydroxyphenyl-Pyruvate Dioxygenase (HPPD) Inhibitors Cumulative Risk Assessment: Benzobicyclon, Bicyclopyrone, Isoxaflutole,

Mesotrione, Pyrasulfotole, Tembotrione, Tolpyralate, and Topramezone,” which is available in the docket for the action, and concluded that cumulative exposures to HPPD inhibitors (based on proposed and registered pesticidal uses at the time the assessment was conducted) did not present risks of concern.

Safety Factor (SF) for Infants and Children. The Food Quality Protection Act (FQPA) section has been updated since the last assessment. EPA has determined that the required FQPA SF of 10X for the protection of infants and children be reduced to 1X for all exposure scenarios for benzobicyclon (parent). For metabolite B, since the chronic dietary endpoint is based on a study with no No-Observed-Adverse-Effect Level (NOAEL), a 10X FQPA SF/Uncertainty Factor (UF_L) has been retained for extrapolation from a Lowest-Observed-Adverse-Effect Level (LOAEL) to a NOAEL.

Completeness of the Toxicology Database: The existing toxicological database for benzobicyclon is adequate for FQPA evaluation. Developmental and two-generation reproduction studies in rats are available for benzobicyclon. However, the active moiety of benzobicyclon, metabolite B, has been shown to be more toxic than the parent compound. Therefore, studies were conducted with metabolite B, including a developmental toxicity study in mice. Additionally, 2-generation reproduction toxicity studies are available from other HPPD inhibitors for bridging.

Evidence of Neurotoxicity: There was no neurotoxicity observed throughout the database for benzobicyclon or metabolite B. The subchronic neurotoxicity study with benzobicyclon tested up to 1,290 mg/kg with no adverse effects observed, nor was there evidence of neurotoxicity in any of the guideline studies in the databases for either chemical.

Evidence of Sensitivity/Susceptibility in the Developing or Young Animal: For benzobicyclon, there was no increased qualitative or quantitative susceptibility observed in the two-generation reproduction or developmental toxicity studies in rats. A

developmental study in rabbits was submitted but was considered unacceptable and subsequently waived by EPA.

For metabolite B, a developmental toxicity study in mice did not show any increased qualitative or quantitative susceptibility. A 2-generation reproduction study is not available for metabolite B; however, there are 2-generation reproduction studies from other HPPDs inhibitors that can be used for bridging. In one of the 2-generation studies in mice for another HPPD inhibitor (mesotrione), quantitative susceptibility was observed in offspring. However, concern is low because there are clear NOAEL/LOAEL values for the observed effects, the offspring LOAEL of 300 mg/kg/day from the mesotrione 2-generation reproduction toxicity study was set conservatively based on a low incidence of opaque/cloudy eyes, and the selected endpoints used in this risk assessment are protective of any potential sensitivity observed in mice.

Residual Uncertainty in the Exposure Database: The exposure databases are complete or are estimated based on data that reasonably account for potential exposures. There are no registered or proposed residential uses and/or commercial uses at residential sites for benzobicyclon at this time. Therefore, a residential exposure assessment is not required. The dietary exposure assessments (food and drinking water) are considered to be conservative estimates of exposure. Tolerance-level residues for rice and 100 PCT were assumed for the food exposure assessment. Drinking water exposure estimates (for both benzobicyclon and metabolite B) are based on conservative models assuming maximum use rates and are not expected to underestimate the exposure. The Agency is confident that the assessments do not underestimate risk from dietary exposure to benzobicyclon or metabolite B.

Aggregate risks and Determination of safety. EPA determines whether acute and chronic dietary pesticide exposures are safe by comparing aggregate exposure estimates to the acute population-adjusted dose (aPAD) and the chronic population-adjusted dose

(cPAD). Short-, intermediate-, and chronic term risks are evaluated by comparing the estimated aggregate food, water, and residential exposure to the appropriate points of departure to ensure that an adequate margin of exposure (MOE) exists. For linear cancer risks, EPA calculates the lifetime probability of acquiring cancer given the estimated aggregate exposure.

There are no acute dietary endpoints for benzobicyclon or metabolite B; therefore, an acute risk assessment is unnecessary. Chronic dietary risks are below the Agency's level of concern of 100% of the cPAD for both benzobicyclon and metabolite B. It is less than 1% of the cPAD for benzobicyclon for all population subgroups and 5.8% of the cPAD for metabolite B for all infants less than 1-year old, the population subgroup with the highest exposure estimate for both benzobicyclon and metabolite B.

As noted earlier, there are no residential uses associated with benzobicyclon. Because there is no short- or intermediate-term residential exposure and chronic dietary exposure has been assessed under the appropriately protective cPAD, EPA relies on the chronic dietary risk assessment for evaluating short- and intermediate-term risk for benzobicyclon and metabolite B.

Based on the lack of evidence of carcinogenicity in two adequate rodent carcinogenicity studies, benzobicyclon is not expected to pose a cancer risk to humans. For metabolite B, potential carcinogenicity is not a concern for the HPPD inhibitors and the chronic dietary endpoint and POD for metabolite B is considered protective of any potential carcinogenicity.

Therefore, based on the risk assessments and information described above, EPA concludes there is reasonable certainty that no harm will result to the general population, or to infants and children, from aggregate exposure to benzobicyclon or metabolite B residues. More detailed information can be found at <http://www.regulations.gov> in the

Benzobicyclon Human Health Risk Assessment in docket ID number EPA-HQ-OPP-2020-0391.

IV. Other Considerations

A. Analytical Enforcement Methodology

For a discussion of the available analytical enforcement method, see Unit IV.A. of the April 25, 2017 rulemaking (82 FR 18995) (FRL-9961-02).

B. International Residue Limits

In making its tolerance decisions, EPA seeks to harmonize U.S. tolerances with international standards whenever possible, consistent with U.S. food safety standards and agricultural practices. EPA considers the international maximum residue limits (MRLs) established by the Codex Alimentarius Commission (Codex), as required by FFDCA section 408(b)(4).

The Codex has not established an MRL for residues of benzobicyclon in or on rice grain.

V. Conclusion

Therefore, the tolerance for residues of benzobicyclon on rice, grain is increased from 0.01 ppm to 0.15 ppm and is no longer a tolerance with regional restrictions.

VI. Statutory and Executive Order Reviews

This action increases a tolerance under FFDCA section 408(d) in response to a petition submitted to the Agency. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled “Regulatory Planning and Review” (58 FR 51735, October 4, 1993). Because this action has been exempted from review under Executive Order 12866, this action is not subject to Executive Order 13211, entitled “Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use” (66 FR 28355, May 22, 2001), or to Executive Order 13045, entitled “Protection of Children from Environmental Health

Risks and Safety Risks” (62 FR 19885, April 23, 1997). This action does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (PRA) (44 U.S.C. 3501 et seq.), nor does it require any special considerations under Executive Order 12898, entitled “Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations” (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCFA section 408(d), such as the tolerance in this final rule, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (RFA) (5 U.S.C. 601 et seq.), do not apply.

This action directly regulates growers, food processors, food handlers, and food retailers, not States or Tribes, nor does this action alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCFA section 408(n)(4). As such, the Agency has determined that this action will not have a substantial direct effect on States or Tribal Governments, on the relationship between the National Government and the States or Tribal Governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian Tribes. Thus, the Agency has determined that Executive Order 13132, entitled “Federalism” (64 FR 43255, August 10, 1999) and Executive Order 13175, entitled “Consultation and Coordination with Indian Tribal Governments” (65 FR 67249, November 9, 2000) do not apply to this action. In addition, this action does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act (UMRA) (2 U.S.C. 1501 et seq.).

This action does not involve any technical standards that would require Agency consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act (NTTAA) (15 U.S.C. 272 note).

VII. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq.*), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the *Federal Register*. This action is not a “major rule” as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides, and pests, Reporting and recordkeeping requirements.

Dated: October 27, 2021

Marietta Echeverria,

Acting Director, Registration Division, Office of Pesticide Programs.

Therefore, for the reasons stated in the preamble, EPA is amending 40 CFR chapter 1 as follows:

PART 180—TOLERANCES AND EXEMPTIONS FOR PESTICIDE CHEMICAL RESIDUES IN FOOD

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

2. Revise § 180.693 to read as follows:

§ 180.693 Benzobicyclon; tolerances for residues.

(a) *General.* Tolerances are established for residues of the herbicide benzobicyclon, including its metabolites and degradates, in or on the commodity in the table below. Compliance with the tolerance level specified below is to be determined by measuring only benzobicyclon, 3-[2-chloro-4-(methylsulfonyl)benzoyl]-4-(phenylthio)bicyclo-[3.2.1]oct-3-en-2-one), in or on the following raw agricultural commodity:

Table 1 to § 180.693(a)

Commodity	Parts per million
Rice, grain	0.15

(b) – (d) [Reserved]

[FR Doc. 2021-23836 Filed: 11/1/2021 8:45 am; Publication Date: 11/2/2021]